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13.5
Vertebrate Animals Used in Research

Recommended for approval by the ES&H Working Group

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13.5

Vertebrate Animals Used in Research*

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* **New document**

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Vertebrate Animals Used in Research

1.0 Introduction

1.1 Program Description

Lawrence Livermore National Laboratory is required by federal law to review and approve all research projects involving vertebrate animals. The Laboratory adopts the requirements in the Animal Welfare Act of 1968 (i.e., 7 USC 2131–2157, as amended), as established by the Department of Health and Human Services (DHHS). LLNL also voluntarily adheres to the guidelines for the use of vertebrate animals in research established by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International.

1.2 Purpose and Scope

The LLNL Institutional Animal Care and Use Committee (IACUC) was established and is supported by the Laboratory Director as part of his assurance to the DHHS that LLNL complies with federal regulations pertaining to the protection of vertebrate animals involved in research projects at the Laboratory. The Laboratory Director has delegated responsibility for the oversight of research involving vertebrate animals to the Associate Director for the Biology and Biotechnology Research Program (BBRP).

This document contains key information about the IACUC and federal regulations that govern the use of live vertebrate animals in research activities. (See Appendix A for the definitions of relevant terms.) All vertebrate animal research shall be reviewed and approved by the IACUC, which also provides additional information for researchers who are using, or contemplating the use of, vertebrate animals in their research projects. The IACUC Office, which supports the IACUC, keeps abreast of all rules and regulations relevant to the use of vertebrate animals in research and should be consulted when questions arise.

In addition, the Office of Laboratory Animal Welfare [of the National Institutes of Health (NIH)] maintains an extensive Web site listing policies, laws, guidance, general information, and links to other Web sites relevant to the care and use of vertebrate animals in research. Refer to the following Internet address:

http://grants.nih.gov/grants/olaw/olaw.htm

1.3 General Requirements

All research involving vertebrate animals shall be reviewed and approved by the IACUC whether or not such animals are maintained onsite. This requirement applies to all other activities that even in part involve such research, regardless of sponsorship, if one or more of the following apply:

- The activity is sponsored, in part or entirely, by LLNL.
- Some or all of the activity is conducted by, or under the direction of, any LLNL employee or subcontract worker in connection with his or her LLNL duties.
- Some or all of the activity is conducted using any LLNL property or facility.

The term "vertebrate animal research" covers a broad range of activities. The following list provides a few examples of activities that may require IACUC review and approval:

- Seeking or obtaining information on vertebrate animals directly, i.e., through experiments conducted at LLNL.
- Collaborative studies in which material or information from vertebrate animals is collected at another institution and sent to researchers at the Laboratory.
- Donation of tissue, organs, fluids, or other vertebrate animal material obtained from other investigators.
- Physical participation in an activity involving vertebrate animals.
- Evaluation of veterinary or medical devices intended to evaluate health or detect disease.

2.0 Hazards

Vertebrate animal research involves hazards that vary with the specific research protocol and the type of animal being used. It is imperative that Responsible Individuals be aware of hazards in their research protocols and develop safeguards to protect researchers and animal handlers from those hazards.

The unique hazards of work involving vertebrate animals include bites and scratches, which pose the potential of contracting an animal-transmitted disease. Development of allergic responses to animals may also occur. LLNL maintains a comprehensive occupational health and safety program to protect individuals working with animals. Employees with regular exposure to animals shall be enrolled in a medical surveillance program through the Health Services Department. Appendix B gives basic safety

information for working with vertebrate animals. Appendix C provides basic worker safety information for the necropsy of infected animals. Appendix D covers steps to take to prevent asthma in animal handlers. In addition to the information in Appendices B, C, and D, hazard-specific requirements may also be found in safety plans or other project-specific documentation [e.g., Integration Work Sheets (IWSs) and Hazard Assessment and Control (HAC) Forms].

For requirements and information regarding other personnel safety issues that are related to laboratory research activities and that are beyond the scope of this document, contact your Environment, Safety, and Health (ES&H) Team. In addition, refer to other *ES&H Manual* documents, such as the following:

- Document 13.1, "Biological Controls and Operations."
- Document 14.1, "Chemicals."
- Document 14.12, "Safe Handling of Carcinogenic Materials."
- Document 20.1, "Occupational Radiation Protection."

Researchers also bear the ultimate ethical responsibility for their work with vertebrate animals. Society entrusts researchers with the privilege of using animals to advance scientific knowledge. In return, society expects researchers to show respect for animal subjects. Keeping this in mind, Responsible Individuals shall consider the potential for hazards associated with the administration of chemicals and radiation to animals.

3.0 Controls

All research projects involving vertebrate animals require formal review and approval by the IACUC. The following are among the topics considered in the review of animal protocols:

- Rationale and purpose of the proposed use of animals.
- Justification of the species and number of animals requested.
- Availability or appropriateness of less-invasive procedures or alternative species or approaches for the experimental question.
- Adequacy of training and experience of personnel in the procedures used.
- Housing and husbandry requirements.
- Sedation, analgesia, and anesthesia.
- Unnecessary duplication of experiments.

- Postprocedural care of animals.
- Safety of the working environment for personnel.

Ongoing reporting requirements also apply to all vertebrate animal research activities. All vertebrate animal research projects shall follow the Animal Welfare Act and the *Guide for the Care and Use of Laboratory Animals* (see Section 6.3).

3.1 Submitting a Protocol Application for IACUC Review

Prior to preparing a protocol application for review, the Responsible Individual should consult the IACUC Office and discuss the following issues with IACUC Office personnel:

- The type of review required.
- Any documentation necessary for the review.
- The review schedule.

There are three types of IACUC review: full Committee review, expedited review, and collaboration review. Each type of review is discussed below. The primary responsibility for determining the most appropriate type of review rests with the IACUC Chair. Most projects will require full committee review. (Some activities involving vertebrate animals may qualify for exemption from review. For more information, see Section 3.2.)

Full Committee Review

A full Committee review takes place at a convened meeting of the IACUC at which a quorum of Committee members are in attendance.

Expedited Review

A vertebrate animal research project that requires prompt approval may qualify for expedited review. In an expedited review, which takes place outside of (i.e., does not require) a convened meeting at which a quorum of Committee members are in attendance, a submitted research proposal is made available to all Committee members to review and is required to be reviewed by at least two members. The IACUC Chair collects comments submitted by IACUC members and notifies the requestor of any changes that need to be made in the proposal. A revised proposal is then submitted to the IACUC Chair, who decides whether to approve the proposal.

A protocol that is not suitable for an expedited review is reviewed by the full Committee during a regularly scheduled IACUC meeting.

Collaboration Review

"Collaboration," as used in this document, refers to cases in which an LLNL investigator receives animal tissue, organs, or fluids from another LLNL investigator, or from a nonLLNL investigator, under an approved animal use protocol. In some cases of such studies, the appropriate form (see Section 6.2), rather than a full protocol proposal, may be submitted to the IACUC Chair.

3.2 Research Activities Exempt from Federal Regulations

If the vertebrate animal involvement in a research project satisfies certain criteria, and the Responsible Individual believes the research activity is exempt from federal regulations governing research on vertebrate animals, the Responsible Individual shall contact the IACUC Office to request exemption. If the research activity is determined by the IACUC Office to be exempt from further review, the Office issues a letter stating this fact to the requestor. However, research activities thus determined to be exempt from federal requirements are not exempt from other requirements or guidelines specified in this document.

3.3 Continuing Reviews

All research using vertebrate animals shall receive continuing review on at least an annual basis, i.e., at an interval not to exceed twelve months. Research involving novel or untested procedures may require more frequent review, as determined by the IACUC.

3.4 Ongoing Reporting for Previously Approved Research

After a protocol has been approved, the Responsible Individual has ongoing reporting responsibilities and shall obtain written approval from the IACUC for all changes to the protocol before any such changes can be implemented. For example, an amended protocol is required when the investigator proposes to involve vertebrate animals in ways different from those approved in the original protocol. IACUC review and approval are also required in the event of changes in the type of animal or increases in the number of animals initially approved by the IACUC.

3.5 Training

All researchers at LLNL who are engaged in vertebrate animal research shall successfully complete training appropriate for their proposed work. Because much of the work on animals is unique to each protocol, appropriate training is provided or specified by the IACUC Office on an as-needed basis.

4.0 Responsibilities

General responsibilities for all workers are described in Document 2.1, "Laboratory and ES&H Policies, General Worker Responsibilities, and Integrated Safety Management," in the *ES&H Manual*.

LLNL, the IACUC, the IACUC Office, and Responsible Individuals share responsibility for the proper review of research using vertebrate animals. The responsibilities of each are described in this section.

4.1 BBRP Associate Director (Authorized Institutional Official)

The LLNL Director has designated the BBRP Associate Director as the Authorized Institutional Official (AIO). The AIO is responsible for the performance of all LLNL research involving vertebrate animals. The AIO also agrees to maintain the IACUC and provide meeting space and staff to support the IACUC's review and recordkeeping duties.

4.2 Institutional Animal Care and Use Committee Office

The IACUC Office is responsible for:

- Facilitating interactions between the IACUC and researchers.
- Determining the most appropriate type of IACUC review (i.e., expedited review, full Committee review, or collaboration review) for each research activity or whether the activity is exempt from review.
- Maintaining IACUC records and acting as the point of contact for external audits.
- Interacting with governmental departments and agencies, the AAALAC, and other IACUCs in matters regarding vertebrate animal research.
- Providing, or referring personnel to sources of, information and education concerning regulations and guidelines covering research involving vertebrate animals.
- Staying abreast of relevant rules and regulations.
- Assuring that appropriate animal-care training is available.

4.3 Institutional Animal Care and Use Committee

The IACUC is responsible for ensuring that a research activity involving vertebrate animals includes processes for protecting the welfare of animals by:

- Evaluating proposed research activities.
- Approving or requiring modification to research protocols.
- Conducting continuing review of active protocols (at least annually).
- Conducting semiannual inspections of animal-care facilities and operations.

4.4 Responsible Individual's Supervisor

Responsible Individuals (i.e., investigators) are required to provide the name of their supervisor on any application to the IACUC. The primary responsibilities of the Responsible Individual's supervisor are to:

- Be aware of the vertebrate animal research activities that occur within his or her program.
- Ensure that all appropriate reviews and other controls are properly implemented.

The IACUC Office provides a copy of the IACUC approval letter to the supervisor, if requested.

4.5 Responsible Individuals

Responsible Individuals are responsible for:

- Protecting the welfare of vertebrate animals used in their research.
- Notifying the IACUC of their intention to use vertebrate animals in research.
- Submitting to the IACUC material (including forms, listed in Section 6.2) required to facilitate a review of the research.
- Understanding and adhering to the ethical standards and regulatory requirements governing the research activities.
- Recognizing that IACUC review and approval shall precede initiation of any work involving vertebrate animals.
- Requesting and obtaining IACUC approval of any changes to a research protocol prior to implementation of those changes.

- Ensuring a safe and healthful workplace for workers.
- Providing the names of individuals who are exposed to animals to payroll supervisors so that the individuals may be enrolled in medical surveillance and receive proper training.

4.6 Payroll Supervisors

Payroll supervisors shall:

- Assure that individuals working with animals have received the necessary training.
- Enroll individuals who are exposed to animals in a medical surveillance program through the Health Services Department.

4.7 Health Services Department

The Health Services Department shall maintain a medical surveillance program for individuals who are exposed to animals and provide treatment for individuals with medical problems related to animal exposure.

5.0 Work Smart Standards

7 USC 2131–2157, "Transportation, Sale and Handling of Certain Animals" (also known as the Animal Welfare Act) (only portions that apply to the use of animals in research).

Public Law 99-158, Health Research Extension Act of 1985.

6.0 Resources for More Information

6.1 General Information

Information about the Laboratory's IACUC and vertebrate animal research can be obtained by contacting the IACUC Office.

6.2 Forms

Table 1 lists the forms that investigators submit to the IACUC Office when requesting new or continuing review of a research activity involving vertebrate animals. Electronic versions of the forms are available from the IACUC Office.

Table 1. Forms to submit for reviews of research involving vertebrate animals.

Type of activity	Form to submit
New protocol	"**Protocol for Experimental Use of Live Vertebrate Animals**"
Annual review	"**Protocol for Experimental Use of Live Vertebrate Animals**"
Protocol amendment or modification	"**Protocol for Experimental Use of Live Vertebrate Animals**"
Research collaboration	**The appropriate collaboration form:** "**Animal Tissue Use Involving LLNL and NonLLNL Investigators**" **OR** "**Animal Tissue Use Involving Two LLNL Investigators**"

6.3 Other Sources

Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International. Refer to the following Internet address:
http://www.aaalac.org

Guide for the Care and Use of Laboratory Animals, National Research Council, National Academy Press, Washington, DC. Refer to the following Internet address:
http://www.nap.edu/books/0309053773/html/index.html

Office of Laboratory Animal Welfare, NIH. Refer to the following Internet address:
http://grants.nih.gov/grants/olaw/olaw.htm

UC Davis Web site, "Occupational Health and Animals." Refer to the following Internet address:
http://clueless.ucdavis.edu/health/index.html

Appendix A

Acronyms, Terms, and Definitions

AAALAC	Association for Assessment and Accreditation of Laboratory Animal Care.
AIO	See "Authorized Institutional Official."
Authorized Institutional Official	The individual designated by the LLNL Director as required by the AAALAC.
BBRP	Biology and Biotechnology Research Program.
DHHS	Department of Health and Human Services.
Institutional Animal Care and Use Committee (IACUC)	An institutional committee established in accordance with, and for the purposes expressed in, the regulations and standards listed in Section 5.0 of this document.
IACUC	See "Institutional Animal Care and Use Committee."
NIH	National Institutes of Health.
Research	A systematic investigation, including development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. This definition extends to pilot studies and service programs.
Vertebrate animal	A living animal with a backbone (i.e., spinal column).

Appendix B

Basic Safety for Animal Handling

The following information [adapted from the UC Davis Occupational Health Web site (http://clueless.ucdavis.edu/health/StayingHealthy.html)] is to promote personnel safety when handling vertebrate animals:

- Wash hands.

  The most common way of contracting an animal-transmitted infection is placing the infectious material directly into the mouth.

  Workers shall always wash their hands after handling an animal or anything that an animal has touched. Never smoke, drink, or eat in an animal area or before washing hands.

- Wear protective clothing.

  Workers shall always wear the appropriate protective clothing (e.g., a disposable lab coat) when working with animals. Never take protective clothing home. Protective clothing helps prevent potentially contaminated material from leaving an animal area. Refer to the safety plan, IWS, HAC Form, or other documentation for required protective clothing.

- Use personal protective equipment (PPE).

  Workers shall wear the appropriate PPE (e.g., gloves, face shields, masks, and respirators) when required and follow their supervisor's instructions scrupulously. Refer to the safety plan, IWS, HAC form, or other documentation for required protective clothing.

- Participate in medical surveillance.

  The Health Services Department provides appropriate testing, immunizations, and periodic screening for allergies, infections, and other medical problems related to animal exposure.

- Seek medical attention promptly when injured.

  Workers who are injured on the job shall promptly inform their supervisor (even if the injury seems relatively minor), then report to the Health Services Department for evaluation and treatment of the injury. Refer to Document 10.1, "LLNL Occupational Medical Program," in the *ES&H Manual*.

- Inform physicians of work involving vertebrate animals.

  Workers engaged in work involving vertebrate animals should inform their physician of the work when seeking treatment for illness, even if uncertain

whether the illness is work related. If there is any possibility of work-related illness or disease, the Health Services Department shall be notified immediately. Employees should also inform their personal physicians about any animal exposure when seeking medical attention. Physicians need such information to make an accurate diagnosis because many animal-transmitted diseases have flulike symptoms.

- Get answers to questions.

  Workers should always ask their supervisor about anything they do not understand. Furthermore, LLNL organizations that desire a formal training class on animal-transmitted diseases or other occupational health issues should contact their ES&H Team or the Health Services Department.

- Get the appropriate training.

  All at-risk persons working in a facility where animals are kept shall receive appropriate training on that facility's particular biohazards, precautions, and biohazard evaluation procedures. Training includes on-the-job training (OJT), briefings, safety talks, and formal courses. Supervisors are responsible for ensuring that workers are properly trained to perform their job safely and effectively.

  Laboratory workers and animal care personnel are trained to recognize hazard warning signs, to protect themselves and their coworkers against each recognized hazard, and to react properly in the event of emergencies.

  Training shall be documented in accordance with Document 40.1, "LLNL Training Program Manual," in the *ES&H Manual.*

Appendix C

Basic Safety for the Necropsy of Infected Animals

The following information [adapted from *NIH Laboratory Safety Monograph: A Supplement to the NIH Guidelines for Recombinant DNA Research* (July 1978)] is to promote personnel safety during the necropsy of infected animals:

- Ensure that necropsy of infected animals is carried out in biological safety cabinets by trained personnel.
- Wear surgeons' wraparound gowns over laboratory clothing.
- Wear rubber gloves.
- Wet the fur of the animal with a suitable disinfectant.
- Pin down or otherwise fasten small animals to wood or metal in a tray.
- Before and after necropsy, disinfect the inside of biological safety cabinets and other potentially contaminated surfaces with a suitable germicide.
- Upon completion of necropsy, place all potential biohazardous materials in suitable containers, then sterilize the materials.
- Segregate contaminated mixed waste and store for appropriate disposal.
- Place contaminated instruments in a horizontal bath that is located within the biological safety cabinet and contains a suitable disinfectant.
- Clean contaminated rubber gloves in disinfectant before removal from the hands. After removal, check the gloves for holes, then sterilize for reuse or decontaminate prior to disposal. Wearing gloves is not a substitute for hand-washing; wash hands after necropsy and carcass disposal.
- For disposal of dead animals
    1. Place the dead animals into a plastic bag.
    2. Seal the end of the bag by taping or tying into a knot.
    3. Place the bag into a second plastic bag, and close that bag.
    4. Fill out a cardboard tag (with string attached) with the date, name of the investigator, species of animal, number of animals, name of the agent with which the animals are infected, amount of agent that the animals received.
    5. Tie the tag around the neck of the plastic bag.
    6. Place the tagged bag in a plastic-lined, properly labeled cardboard box in the appropriate freezer in the animal care facility.
    7. Enter all relevant information into the freezer log book.
    8. Properly package filled boxes for removal by the Hazardous Waste Management Division and shipment to a contract agency for appropriate disposal.

Appendix D

Preventing Asthma in Animal Handlers

Because exposure to animals and animal products can cause asthma and allergies, the guidelines below [adapted from *Preventing Asthma in Animal Handlers*, DHHS (NIOSH) Publication No. 970-116, January 1998] were developed to protect animal handlers from exposure:

- Perform animal manipulations within ventilated hoods or safety cabinet when possible to avoid exposure to airborne allergenic material.
- Keep cages and animal areas clean.
- Reduce contact with animal products such as dander, serum, and urine by using
  - Gloves.
    A disposable laboratory coat.
    A faceshield, when required.
  - A particulate respirator, when required.
- Maintain an adequate ventilation rate and humidity level in animal housing areas.
- Provide the best filtration possible for recycled air, including considering the use of filter-top cages.
- Ventilate animal housing and handling areas separately from the rest of the facility.
- Direct airflow away from workers and toward the backs of animal cages.
- Minimize animal density (i.e., the number of animals per cubic meter of room volume).
- For bedding, use absorbent pads or (when pads are not available) corncob, rather than sawdust.
- Use an animal species or sex that is known to be less allergenic than others.
- Limit access to animal care areas.

LLNL provides

- Training to educate workers about animal allergies and steps for risk reduction.
- Medical surveillance for employees who have animal exposure.
- Appropriate counseling and medical follow-up for workers who have become sensitized or have developed allergy symptoms.